

CLAIMS

What is claimed is:

- 5 1. A combination pharmaceutical agent for the treatment of an HCV infection comprising a compound effective to inhibit the function of the HCV NS5A protein and another compound having anti-HCV activity.
2. The combination of Claim 1 wherein the other compound having anti-HCV
10 activity is an interferon.
3. The combination of Claim 2 wherein the interferon is selected from the group consisting of interferon alpha 2B, pegylated interferon alpha, consensus interferon, interferon alpha 2A, lymphoblastiod interferon tau.
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4. The combination of Claim 1 wherein the other compound having anti-HCV activity is selected from the group consisting of interleukin 2, interleukin 6, interleukin 12, a compound that enhances the development of a type 1 helper T cell response, interfering RNA, anti-sense RNA, Imiqimod, ribavirin, an inosine 5'-
20 monophosphate dehydrogenase inhibitor, amantadine, and rimantadine.
5. The combination of Claim 1 wherein the other compound having anti-HCV activity is a small molecule.
- 25 6. The combination of Claim 1 wherein the other compound having anti-HCV activity is effective to inhibit the function of a target selected from the group consisting of HCV metalloprotease, HCV serine protease, HCV polymerase, HCV helicase, HCV NS4B protein, HCV entry, HCV assembly, HCV egress, HCV NS5A protein, IMPDH and a nucleoside analog for the treatment of an HCV infection.
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7. The combination of Claim 1 wherein the other compound having anti-HCV activity is effective to inhibit the function of a target in the HCV life cycle other than the HCV NS5A protein.

8. The combination of Claim 1 wherein the compound effective to inhibit the function of the HCV NS5A protein and the other compound having anti-HCV activity are each formulated as separate compositions.

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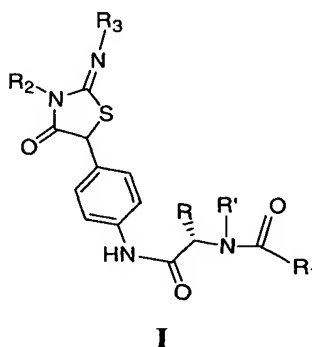
9. The combination of Claim 1 wherein the compound effective to inhibit the function of the HCV NS5A protein and the other compound having anti-HCV activity are to be administered at the same time.

10. The combination of Claim 1 wherein the compound effective to inhibit the function of the HCV NS5A protein and the other compound having anti-HCV activity are to be administered at different times.

11. The combination of Claim 1 wherein the compound effective to inhibit the function of the HCV NS5A protein is a small molecule.

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12. The combination of Claim 11 wherein the small molecule compound is a compound of formula I



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wherein R is C₁₋₄ alkyl, optionally substituted with 1-3 halogen atoms, 1-3 oxygen atoms or 1-3 nitrogen atoms, said R having an S stereoconfiguration; R' is H or a bond wherein R and R' are joined to form a cyclic structure;

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R₁ is a member selected from the group consisting of C₁₋₆ alkyl,

C₃₋₇ cycloalkyl, C₆₋₁₀ aryl, C₁₋₆ alkoxy, C₆₋₁₀ aryloxy, C₆₋₁₀ aryl (C₁₋₆) alkyl, C₆₋₁₀ aryl (C₁₋₆) alkoxy, aryl-substituted C₁₋₆ alkyl (C₆₋₁₀) aryl and Het; and

R₂ and R₃ are each independently selected from the group consisting of C₁₋₆ alkyl, C₃₋₇ cycloalkyl, C₆₋₁₀ aryl, C₁₋₆ alkoxy, C₆₋₁₀ aryloxy, Het, C₆₋₁₀ aryl (C₁₋₆) alkyl, C₆₋₁₀ aryl (C₁₋₆) alkoxy, acyl (C₁₋₆) alkoxy, with the proviso that one of R₂ or R₃ can be a bond and R₂ and R₃ are joined to form a cyclic structure;

or pharmaceutically acceptable enantiomer, diastereomer, solvate, prodrug or salt thereof.

13. The combination of Claim 12 wherein R is methyl.

14. The combination of Claim 12 wherein R is selected from propyl forming a cyclic structure with R', or propionyl forming a cyclic structure with R'.

15. The combination of Claim 12 wherein R₁ is selected from the group consisting of C₆₋₁₀ aryl (C₁₋₆) alkyl, C₆₋₁₀ aryl (C₁₋₆) alkoxy and a 5-7 membered monocyclic heterocycle.

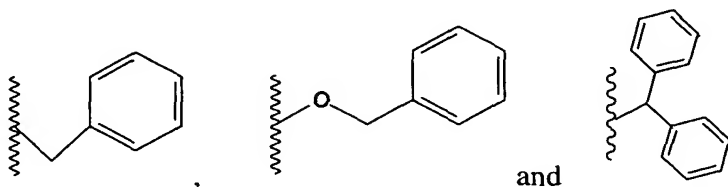
16. The combination of Claim 14 wherein R₁ is selected from the group consisting of C₆ aryl (C₁₋₃) alkyl and C₆ aryl (C₁₋₃) alkoxy.

17. The combination of Claim 12 wherein R₂ and R₃ are each independently related from the group consisting of C₆₋₁₀ aryl, 5-7 membered monocyclic heterocycle, C₁₋₃ alkyl substituted with a 5-7 membered heterocycle, C₆₋₁₀ aryl substituted with a 5-7 membered heterocycle, and a 7-12 membered bicyclic heterocycle.

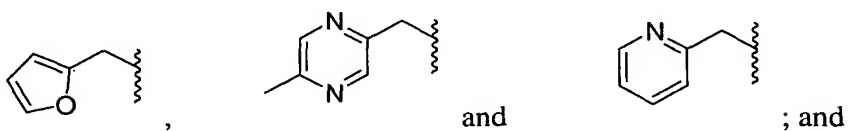
18. The combination of Claim 16 wherein R₂ and R₃ are each independently selected

from a C₁₋₃ alkyl substituted with a 5-7 membered heterocycle and a halogenated 5-7 membered heterocycle.

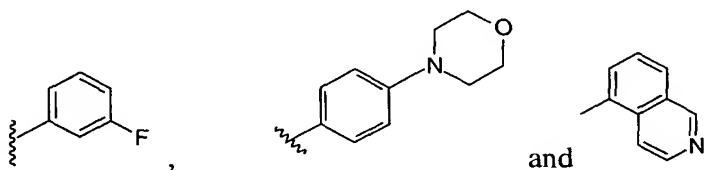
19. The combination of Claim 12 wherein R₁ is selected from the group
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R² is selected from the group consisting of:

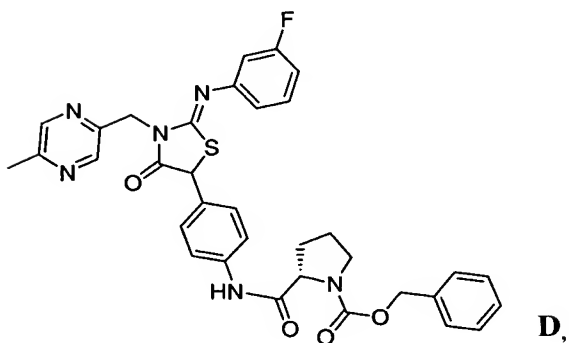
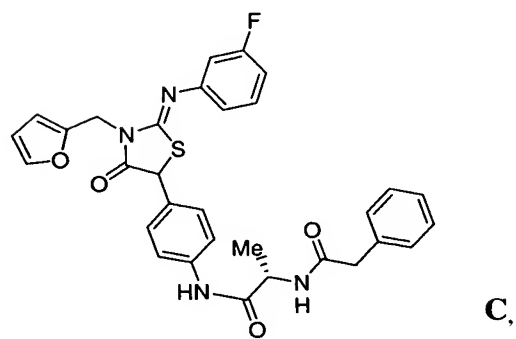
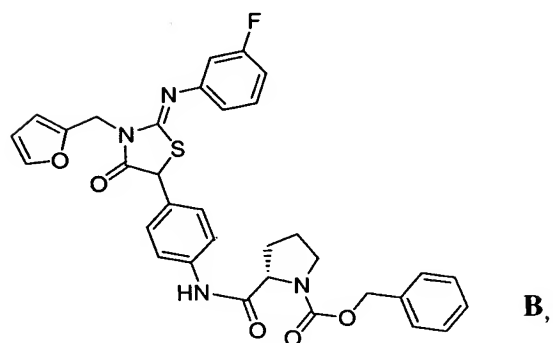
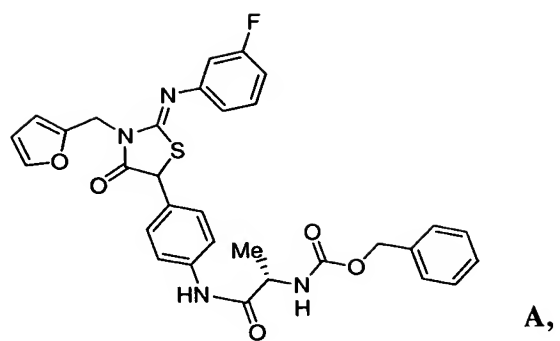


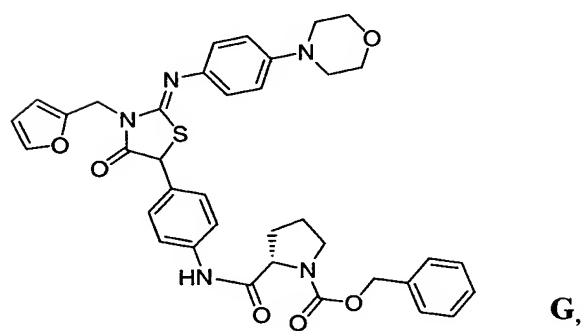
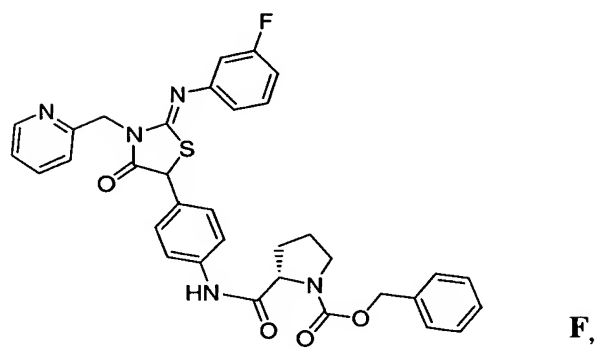
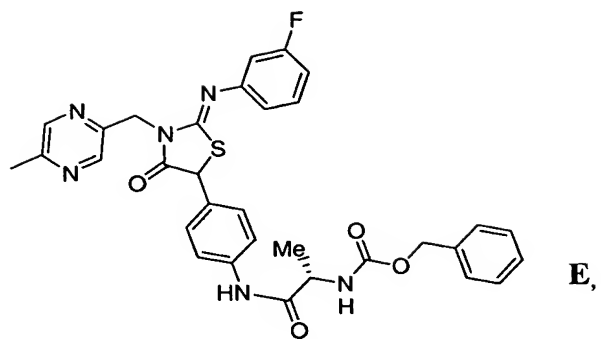
R³ is selected from the group consisting of:

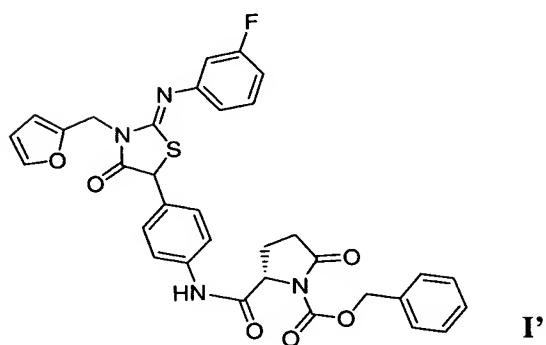
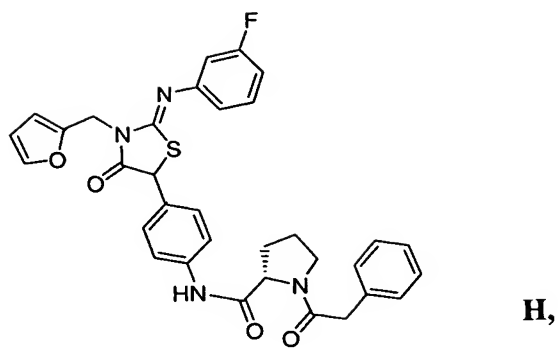


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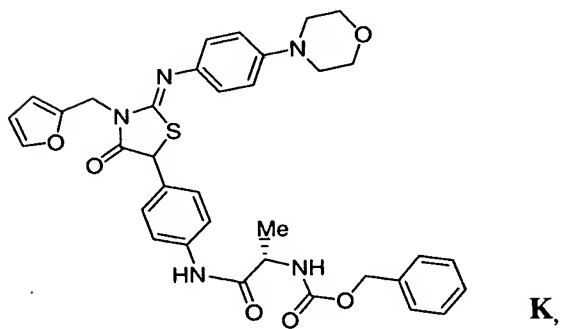
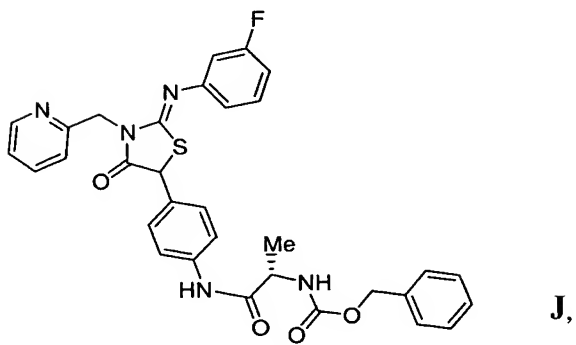
20. The combination of Claim 12 wherein the small molecule compound is
selected
from the group consisting of:

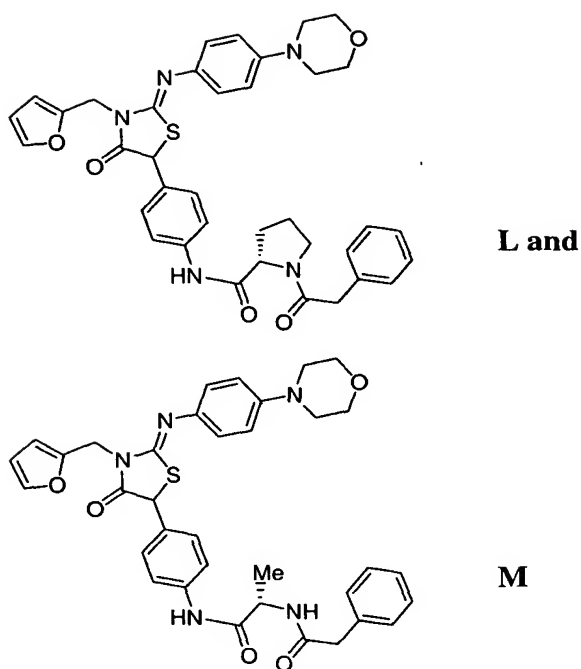






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or pharmaceutically acceptable enantiomer, distereomer, solvate, prodrug or salt thereof.

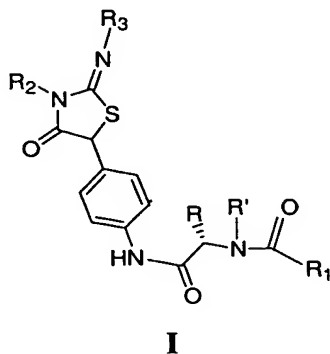
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21. The combination of the compound of formula I and another HCV NS5A inhibitor for concomitant administration for the treatment of an HCV infection.
- 10 22. The combination of the compound of formula I and a HCV metalloprotease inhibitor for concomitant administration for the treatment of an HCV infection.
23. The combination of the compound of formula I and a HCV serine protease inhibitor for
- 15 concomitant administration for the treatment of an HCV infection.
24. The combination of the compound of formula I and a HCV polymerase inhibitor
- for concomitant administration for the treatment of an HCV infection.

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25. The combination of the compound of formula I and a HCV helicase inhibitor for concomitant administration for the treatment of an HCV infection.
- 5 26. The combination of the compound of formula I and a HCV NS4B inhibitor for concomitant administration for the treatment of an HCV infection.
27. The combination of the compound of formula I and a HCV entry inhibitor for
10 concomitant administration for the treatment of an HCV infection.
28. The combination of the compound of formula I and a HCV assembly inhibitor for concomitant administration for the treatment of an HCV infection.
- 15 29. The combination of the compound of formula I and a HCV egress inhibitor for concomitant administration for the treatment of an HCV infection.
30. The combination of the compound of formula I and a an IMPDH inhibitor for concomitant administration for the treatment of an HCV infection.
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31. The combination of the compound of formula I and a nucleoside analog for the treatment of an HCV infection for concomitant administration for the treatment of an HCV infection.
- 25 32. A combination pharmaceutical agent for administration to a patient for the treatment of an HCV infection comprising:
- a) a first pharmaceutical composition comprising a compound effective to inhibit the function of the HCV NS5A protein; and
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- b) a second pharmaceutical composition comprising another compound having anti-HCV activity.

33. The combination of Claim 32 wherein the compound effective to inhibit the function of the HCV NS5A protein is a compound of formula I



wherein R is C₁₋₄ alkyl, optionally substituted with 1-3 halogen atoms, 1-3 oxygen atoms or 1-3 nitrogen atoms, said R having an S stereoconfiguration; R' is H or a bond wherein R and R' are joined to form a cyclic structure;

R₁ is a member selected from the group consisting of C₁₋₆ alkyl, C₃₋₇ cycloalkyl, C₆₋₁₀ aryl, C₁₋₆ alkoxy, C₆₋₁₀ aryloxy, C₆₋₁₀ aryl (C₁₋₆) alkyl, C₆₋₁₀ aryl (C₁₋₆) alkoxy, aryl-substituted C₁₋₆ alkyl (C₆₋₁₀) aryl and Het; and

R₂ and R₃ are each independently selected from the group consisting of C₁₋₆ alkyl, C₃₋₇ cycloalkyl, C₆₋₁₀ aryl, C₁₋₆ alkoxy, C₆₋₁₀ aryloxy, Het, C₆₋₁₀ aryl (C₁₋₆) alkyl, C₆₋₁₀ aryl (C₁₋₆) alkoxy, acyl (C₁₋₆) alkoxy, with the proviso that one of R₂ or R₃ can be a bond and R₂ and R₃ are joined to form a cyclic structure;

or pharmaceutically acceptable enantiomer, diastereomer, solvate, prodrug or salt thereof.

34. The combination of Claim 32 wherein the other compound having anti-HCV activity is an interferon.

35. The combination of Claim 33 wherein the interferon is selected from

the group consisting of interferon alpha 2B, pegylated interferon alpha, consensus interferon, interferon alpha 2A, lymphoblastiod interferon tau.

36. The combination of Claim 32 wherein the other compound having anti-HCV activity is selected from the group consisting of interleukin 2, interleukin 6, interleukin 12, a compound that enhances the development of a type 1 helper T cell response interfering RNA, anti-sense RNA, Imiqimod, ribavirin, an inosine 5'-monophosphate dehydrogenase inhibitor, amantadine, and rimantadine.
37. The combination of Claim 32 wherein the other compound having anti-HCV activity is a small molecule.
38. The combination of Claim 37 wherein the other compound having anti-HCV activity is effective to inhibit the function of a target selected from the group consisting of HCV metalloprotease, HCV serine protease, HCV polymerase, HCV helicase, HCV NS4B protein, HCV entry, HCV assembly, HCV egress, HCV NS5A protein, IMPDH and a nucleoside analog for the treatment of an HCV infection.
39. The combination of Claim 32 wherein the other compound having anti-HCV activity is effective to inhibit the function of a target in the HCV life cycle other than the HCV NS5A protein.